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Abstract

225Ac complexes comprising a functionalized
polyazamacrocyclic chelant compound of the formula I
hereinbelow:

$$G \longrightarrow V$$
 Q
 Q
 Q
 Q

(I)

wherein:

T is

 \nearrow N

G is independently hydrogen or

$$L \xrightarrow{X} (CH_2)_n - C \xrightarrow{V} (CH_2)_r \xrightarrow{V}$$

each Q is independently hydrogen, (CHR $^5)_{\,p}CO_2R$ or (CHR $^5)_{\,p}PO_3R^6R^7$ or

$$L \xrightarrow{\begin{pmatrix} X \\ | \\ C \\ Y \end{pmatrix}_m} (CH_2)_n \xrightarrow{Q^1} (CH_2)_r \xrightarrow{\qquad}$$

 Q^1 is hydrogen, $(CHR^5)_wCO_2R$ or $(CHR^5)_wPO_3R^6R^7$; each R is independently hydrogen, benzyl or C_1 - C_4 alkyl; R^6 and R^7 are independently H, C_1 - C_6 alkyl or $(C_1$ - C_2 alkyl)phenyl;

each R^5 is independently hydrogen; C_1-C_4 alkyl or $(C_1-C_2 \text{ alkyl})$ phenyl;

with the proviso that at least two of the sum of Q and Q^1 must be other than hydrogen;

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A is CH, N, C-Br, C-Cl, C-SO₃H, C-OR⁸, C-OR⁹N⁺-R¹⁰X⁻, or

$$C-C\equiv C-\sqrt{}-R^{11}$$

Z and Z 1 independently are CH, N, C-SO_3H, N $^+-R^{10}X^-$, C-CH_2- OR^{8} or C-C(O)- R^{11} ;

 R^8 is H, $C_1\text{--}C_5$ alkyl, benzyl, or benzyl substituted with 5 at least one R12;

 R^9 is C_1-C_{16} alkylamino;

 R^{10} is $C_1\text{--}C_{16}$ alkyl, benzyl, or benzyl substituted with at least one R^{12} ;

 R^{11} is $-O-(C_1-C_3$ alkyl), OH or NHR¹³; R^{12} is H, NO_2 , NH_2 , isothiocyanato, semicarbazido, 10 thiosemicarbazido, maleimido, bromoacetamido or carboxyl;

 R^{13} is C_1-C_5 alkyl;

 ${\tt X}$ and ${\tt Y}$ are each independently hydrogen or may be taken with an adjacent X and Y to form an additional carbon-15 carbon bond;

n is 0 or 1;

m is an integer from 0 to 10 inclusive;

p is 1 or 2; 20 r is 0 or 1;

w is 0 or 1;

with the proviso that n is only 1 when X and/or Y form an additional carbon-carbon bond, and the sum of r and

w is 0 or 1; 25

L is a linker/spacer group covalently bonded to, and replaces one hydrogen atom of one of the carbon atoms to which it is joined, said linker/spacer group being represented by the formula

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$$R^{1}$$
 Cyc CH_{2}

wherein:

²²⁵Ac.

s is an integer of 0 or 1; t is an integer of 0 to 20 inclusive; R¹ is H or an electrophilic or nucleophilic moiety which 5 allows for covalent attachment to a biological carrier, or synthetic linker which can be attached to a biological carrier, or precursor thereof; and Cyc represents a cyclic aliphatic moiety, aromatic moiety, aliphatic heterocyclic moiety, or aromatic 10 heterocyclic moiety, each of said moieties optionally substituted with one or more groups which do not interfere with binding to a biological carrier; with the proviso that when R¹ is H, the linkage to the biological carrier is through one of Q or Q1; and with 15 the proviso that when R^1 is other than H, at least one of Q and Q^1 must be $(CHR^5)_pPO_3R^6R^7$; and with further proviso that when Q is (CHR⁵)_pCO₂R, Q¹ is (CHR⁵)_wCO₂R, R is H, R^5 is H, and R^1 is H, then the sum of m, n, p, r, s, t, and w is greater than 1; 20 or pharmaceutically acceptable salts thereof; complexed with

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